Screening for microalbuminuria to prevent nephropathy in patients with diabetes: a systematic review of the evidence

Authors' objectives
To evaluate whether screening patients with diabetes for microalbuminuria (MA) is effective according to published criteria (see Other Publications of Related Interest nos.1-2).

Searching
MEDLINE was searched from 1966 onwards and the search strategy was reported. The reference lists of relevant articles and six additional review articles were also checked. Unpublished data were not sought. Only English language publications were included.

Study selection

Specific interventions included in the review
Studies of diagnostic tests for MA were eligible for inclusion if they investigated the testing of un-timed urine samples (i.e. first morning, morning and random urine sampling), where the tests were performed in an ambulatory setting. Studies of quantitative and semi-quantitative tests were included.

Reference standard test against which the new test was compared
No inclusion criteria relating to the reference standard test were stated.

Participants included in the review
Studies in which all the participants were patients with diabetes (type 1 or 2) were eligible for inclusion.

Outcomes assessed in the review
Studies were eligible for inclusion if the sensitivity and specificity of the screening test could be determined from the article.

How were decisions on the relevance of primary studies made?
Articles considered relevant by three of the four reviewers were included.

Assessment of study quality
The quality of the screening articles was graded using published criteria (see Other Publications of Related Interest no.3). The quality of the screening articles was graded by consensus of two reviewers.

Data extraction
The authors did not state how data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis

How were the studies combined?
Pooling of the sensitivities and specificities was considered for: quantitative tests with a cut-off urinary albumin concentration (UAC) of 20 mg/L or greater; the same semi-quantitative test used with any type of urine sample; and the same semi-quantitative test used with one type of urine sample. Pooling was conducted where homogeneity could not be rejected. Confidence intervals (CI) were calculated using the normal approximation to the binomial method.
How were differences between studies investigated?

Between-study homogeneity was investigated using the chi-squared test. The studies were considered homogeneous if the P-value was 0.05 or greater.

Results of the review

Thirty-one articles reporting the performance of one or more MA screening tests were included in the review. Of these, nine (1,691 patients) reported the characteristics of a quantitative test and 23 (8,133 patients) reported the characteristics of a semi-quantitative test. One study reported both.

Screening test performance.

For quantitative tests, where the cut-off UAC was 20 mg/L or greater, the sensitivity ranged from 56 to 100% and the specificity from 81 to 98%. For morning urine samples, the pooled sensitivity was 75% (95% CI: 59, 91) and the pooled specificity was 97% (95% CI: 94, 99). The test performance was similar for all types of urine sample.

For semi-quantitative tests, the sensitivity ranged from 51 to 100% and the specificity from 21 to 100%. The test performance was similar for all types of urine samples.

There is often considerable inter-observer variability in the evaluation of semi-quantitative tests that involve colourimetric changes.

Screening criteria.

Assuming an individual test sensitivity of 90%, a specificity of 90%, and a 10% prevalence of MA, the correlation between tests would have to be lower than 0.1 in order to achieve a positive predictive value of 75% for repeated screening.

Cost information

Five studies estimated the cost-effectiveness of MA screening and treatment with angiotensin-converting enzyme (ACE) inhibitors to prevent end-stage renal disease in patients with type I diabetes. Three of these studies assumed perfect testing for MA and found screening to be cost-saving. The one study that considered false-positive costs found the additional cost of screening for MA, compared with screening for hypertension or macroalbuminuria, to be $27,042 per quality-adjusted life-year (QALY) gained.

The cost-effectiveness of MA screening in patients with type II diabetes, in whom the incidence of end-stage renal disease is lower, was analysed in two studies. These analyses assumed perfect screening characteristics, and one included only Pima Indians who have a higher incidence of end-stage renal disease. MA screening saved QALYs and reduced costs compared with screening for macroalbuminuria, but the routine use of ACE inhibitors for all patients with type II diabetes was more cost-effective ($7,500/QALY).

Authors' conclusions

Screening for MA meets only four of the six Frame and Carlson criteria for evaluating screening tests. The recommended strategies to overcome diagnostic uncertainty by repeat testing are based on expert opinion, are difficult to follow in primary care settings, do not improve diagnostic accuracy sufficiently, and have not been tested in a controlled trial. MA screening tests using random urine sampling have acceptable accuracy but may not be reliable in all settings.

CRD commentary

The review addressed a clear research question using well-defined inclusion criteria. In general, the methods used in the review were adequately described, as were the included primary studies. The limited nature of the literature search, along with the restriction of the review to published, English language studies, might have resulted in the incomplete retrieval of relevant data. The methods used to determine whether measures of diagnostic performance should be
pooled were clearly described and pooling was only conducted where statistically appropriate, but the methods of pooling were not reported. The diagnostic outcome measures of sensitivity and specificity were reported for a diverse range of index tests, but the reference standard(s) of diagnosis was not described. It is therefore difficult to assess the comparability of the studies included in the review. The general nature of the authors’ conclusions, regarding the acceptable accuracy of MA screening using random urine samples, does not appear to follow directly from the evidence presented.

**Implications of the review for practice and research**

*Practice:* The authors did not make any specific recommendations for practice.

*Research:* The authors stated that a practice-based trial comparing screening strategies is needed; strategies incorporating the initial use of a semi-quantitative test with a view to mitigating problems with adherence to repeat screening should be investigated. The question of whether routine prescription of ACE inhibitors is more effective than annual screening and treatment when MA is detected should also be addressed.

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**Other publications of related interest**


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**Record Status**
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